

TRANSPLANTATION RÉNALE / KIDNEY TRANSPLANTATION LIVING DONOR NEPHRECTOMY: OPEN vs LAPAROSCOPY Renal Function and Complications

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Maroun MOUKARZEL¹, Anthony KALLAS CHEMALY¹, Samir RAHHAL¹, Fouad AOUN¹
Fouad NAKHLE², David ATALLAH³, Samir MALLAT⁴, Chebl MOURANI⁵



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ABSTRACT • Objectives: This study is to compare the short and long-term renal function between adult recipients of living laparoscopic and open donors (LR vs OR) to highlight the effect of the surgical technique on graft function. Moreover, we chose to compare the organic (hypertension, proteinuria, serum creatinine) and psychological (aspect of libido, need for anxiolytics) long-term effect of the surgery between laparoscopic and open donors (LD vs OD). **Methods:** After census of adult recipients and living donors between 2003 and 2012, and after application of exclusion criteria and selection of homogeneous groups of donors and recipients, a retrospective cohort study was conducted between October 2008 and January 2012. In recipients, renal function in the short term was reported by the value of serum creatinine at \pm D5 post-op and the long-term values of serum creatinine at 6 and 12 months after surgery. Delayed graft function was defined by a serum creatinine value \geq 2.5 mg/dl on D5 post-op. A questionnaire for donors was established. **Results:** The two groups OR and LR were homogeneous concerning age, sex and body mass index (BMI). Different groups OD and LD, chosen according to the variable of interest, were made homogeneous. Despite a different warm ischemia time between the 2 groups (175.54 seconds in LR vs 44.67 seconds in OR, $p < 0.001$), renal function in the short- and long-term in recipients was not statistically different (At day 5, 1.54 vs 1.50 mg/dl, $p = 0.781$; at 6 months, 1.37 vs 1.38, $p = 0.871$; at 12 months, 1.34 vs 1.36, $p = 0.569$, in OR and LR respectively). Similarly, there was no significant statistical difference concerning organic and psychological complications between OD and LD except for a shorter period between hospital discharge and return to work in LD. **Conclusion:** In our center, renal function in the short- and long-term was similar in OR and LR. Apart from the advantages offered by the laparoscopic technique, organic and psychological long-term effects were similar between OD and LD. Nevertheless, laparoscopy seemed to facilitate kidney donation and is requested by almost all living donors independently of their social status.

Keywords: nephrectomy, open surgery, laparoscopy, living donor

INTRODUCTION

Renal transplantation has had a major impact on survival and quality of life of patients with chronic renal failure. Traditionally, most cases were from cadaveric donors. However, grafts obtained from living donors have better

RÉSUMÉ • Objectifs : Nous avons tenu à comparer la fonction rénale à court et long terme entre les receveurs adultes de donneurs vivants opérés par voie ouverte et laparoscopique (RO vs RL) afin de souligner l'effet de la technique chirurgicale sur la fonction du greffon. De plus, nous avons choisi de comparer à long terme l'effet organique (hypertension, protéinurie, créatinine sérique) et psychique (aspect de la libido, prise d'anxiolytique) de la chirurgie entre les donneurs ouverts et laparoscopiques (DO vs DL). **Méthodes :** Après recensement des receveurs adultes et des donneurs vivants entre 2003 et 2012, et après application des critères d'exclusion et choix de groupes homogènes de donneurs (DO vs DL) et receveurs (RO vs RL), une étude de cohorte rétrospective a été menée entre oct. 2008 et janv. 2012. Chez les receveurs, la fonction rénale à court terme a été rapportée par la valeur de la créatininémie à \pm J5 postop et celle à long terme par les valeurs de la créatininémie à 6 et 12 mois après l'opération. La fonction retardée du greffon a été définie par une valeur de la créatininémie \geq 2,5 mg/dl à J5 postop. Un questionnaire pour les donneurs a été établi. **Résultats :** Les 2 groupes RL et RO étaient homogènes selon l'âge, le sexe et l'indice de masse corporelle (IMC). Les différents groupes DO et DL, choisis selon la variable étudiée, ont été rendus homogènes. Malgré un temps d'ischémie chaude différent entre les 2 groupes (175,54 secondes chez RL vs 44,67 secondes chez RO, $p < 0,001$), la fonction rénale à court et à long terme chez les receveurs étaient statistiquement non différente (À J5, 1,54 vs 1,50 mg/dl, $p = 0,781$; à 6 mois, 1,37 vs 1,38, $p = 0,871$; à 12 mois, 1,34 vs 1,36, $p = 0,569$, chez RO et RL respectivement). De façon similaire, nous n'avons pas noté de différence significative concernant les complications organiques et psychiques entre DO et DL à l'exception d'un retour plus rapide au travail chez DL. **Conclusion :** Dans notre centre, la fonction rénale à court et long terme a été similaire chez les RL et RO. En dehors des avantages connus offerts par la technique laparoscopique au donneur vivant, les complications organiques et psychiques à long terme ont été similaires entre DO et DL. Toutefois, la laparoscopie paraît faciliter la transplantation rénale et est requise pour presque tous les donneurs vivants indépendamment de leur statut social.

results [1]. Recent data indicate that the current renal function and survival of living donor recipients exceed those of cadaveric donors. The survival rate of living donor graft is 95%, 88% and 80% at 1, 3 and 5 years, respectively. This is in comparison with the rate of graft

¹Urology, ³Gynecology-Obstetrics & ⁵Pediatrics Departments, CHU Hôtel-Dieu de France, Saint-Joseph University (USJ), Beirut, Lebanon.
²Faculty of Medical Sciences, USJ ⁴Nephrology Department, American University of Beirut Medical Center, Beirut, Lebanon.
Correspondence: M. Moukarzel, MD. e-mail : marounmoukarzel@gmail.com

survival of cadaveric donors which is 87%, 77% and 65% at 1, 3 and 5 years, respectively. Given the elective nature of renal transplantation from living donors, the medical condition of the donor and recipient can be optimized, which increases the chances of successful transplantation and reduces the duration of hospitalization. In fact, with the living donor kidney transplantation, we have the advantage of a better HLA (human leucocyte antigen) histocompatibility, a shorter cold ischemia time and a smaller dose of immunosuppressants [1]. HLA system is the locus of genes that encode for proteins on the surface of cells that are responsible for regulation of the immune system in humans.

During the years 1995 to 1998, despite the significant advantage of graft from living donor compared to cadaveric donor, kidney transplantation from living donors accounted for only half or even a third of all kidney transplants in the United States [2]. This was due in part to the problems faced by potential donors during nephrectomy: fear of a prolonged hospital stay, fear of postoperative pain, delayed return to work, and the cosmetic incision result in the abdomen or side wall. With the idea of introducing a less invasive surgical technique, the laparoscopic nephrectomy, these problems already mentioned can be avoided and this technique is an alternative to open nephrectomy. In 1995, Ratner and Kavoussi were the first to perform laparoscopic nephrectomy for human living donor and this at the Johns Hopkins Hospital in Baltimore [3]. All subsequent studies have shown that with this technique, laparoscopic donors have fewer days of hospitalization, early return to work and daily activities, have less pain, less need for analgesics and a better cosmetic result [4]. With the adoption of this technique, many renal transplant centers reported an increase in the number of donors. Since then, renal transplantation from living donors accounted for 55% of all transplants [5] in the United States.

However, many doctors and surgeons have questioned the effect of laparoscopic nephrectomy on renal function of the graft. Indeed, the problem to report with this technique is that warm ischemia time is higher and the kidney is subjected to positive intra-abdominal pressure of the pneumoperitoneum. The latter has been shown responsible for a decrease in renal blood flow in animals [6]. Despite these inconvenients, laparoscopic nephrectomy does not seem to present problems regarding the renal function of the graft, and remains relatively safe in the hands of experts. Is it the same in our center? A question we try to answer in our study is whether there's difference in organic and psychological long-term complications between the two groups of donors.

METHODS

The data in our center from January 2003 to January 2012 for adults living kidney donors (open and laparoscopic nephrectomy) and adult recipients (age ≥ 18 years) were reported retrospectively. The cadaveric transplant

recipients and pediatric recipients have been excluded. A retrospective cohort study was conducted from October 2008 to January 2012 with informed consent.

Regarding the selection of recipients, were excluded from the study those who were not under the same immunosuppressive protocol during the first year post-op. Rejection was considered if proven by biopsy; cases of rejection reported during the first year post-op were similarly excluded. Moreover, were not considered in our study recipients who underwent kidney retransplantation and those who died during the first year post-op. Cases of multiple, retro- and circumaortic renal arteries and those of right nephrectomy were also excluded.

Warm ischemia time

The values of warm ischemia time in donors have been reported in seconds.

Renal function in recipients

It was divided into two: the renal function in the short term and that in the long term.

The first was reported by the value of serum creatinine (mg/dl) at \pm D5 post-op. The second was reported by the value of serum creatinine (mg/dl) at 6 and 12 months of operation. Delayed graft function was defined as a serum creatinine ≥ 2.5 mg/dl at \pm D5 post-op.

Long-term organic complications in donors

Were reported the occurrence of hypertension/HTN (if $\geq 140/90$ mmHg), the appearance of proteinuria (qualitative test) and the serum creatinine values (in mmol/l) at one year of operation.

Regarding the variable *HTN*, were excluded from the study • those in whom blood pressure was not measured during medical monitoring in the 1st year post-op, • those in whom we noted the presence of premature cardiovascular disease in 1st degree relatives (male < 55 years, female < 65 years) and • those in whom drug intake may affect blood pressure.

Regarding the variable *Proteinuria*, were excluded from the study those who have not done urinalysis test at 12 ± 2 months post-op (or those who no longer have their results).

Regarding the variable *Creatinine*, were excluded those who have not test their serum creatinine at 12 ± 2 months post-op (or those who no longer have their results).

Quality of life among donors

Have been reported the period between hospital discharge and return to work (weekdays), the necessity of taking anxiolytics and evaluation of the libido at 6 months post-op.

Regarding the variable *Time between hospital discharge and return to work*, were excluded unemployed donors, those who have work involving risk (construction workers, carpenters, mechanics, etc.) and those who were lost to view.

Regarding the variable *Evaluation of libido at 6 months*

TABLE I CHARACTERISTICS of RECIPIENTS SELECTED in the STUDY

Characteristics	Number	Mean age \pm SD (Year)	Body mass index \pm SD (kg/m ²)	Sex of recipients M/F	Sex of corresponding donors M/F
Laparoscopic donor recipients (LR)	36	42.7 \pm 13	24.8 \pm 2.6	17/17	15/13
Open donor recipients (OR)	45	44.2 \pm 14	25.2 \pm 2.4	21/9	12/17
Value of <i>p</i> (LR:OR)	Not significant	Not significant	Not significant	Not significant	Not significant

post-op, were excluded • women already going through menopause before nephrectomy, • those with a problem of libido in pre-op and • those who were lost to view.

Regarding the variable *Taking anxiolytic at 6 months postoperatively*, were excluded • those who had regular use of anxiolytics before donation, • those who have had a significant stressful event during the first six months (death of a friend or a family member, socio-economic failure, etc.) and • those who were lost to view.

Statistical methods

Continuous variables (body mass index, age, serum creatinine, warm ischemia time, time between hospital discharge and return to work) have been reported with their average and compared using Student’s t-test (or t-test) for normally distributed variables and the Wilcoxon-Mann-Whitney (WMW) for those with non-normal distribution. The test used for normality is the Lilliefors test and the normally distributed variables are: serum creatinine in recipients and donors, time between hospital discharge and return to work and body mass index in donors and recipients). The abnormal distribution variables are age of donors and recipients and the warm ischemia time.

Categorical variables (sex, presence of delayed graft-function, occurrence of hypertension, appearance of proteinuria, taking anxiolytic and evaluation of libido) were compared between the two groups by the χ^2 test and Fisher exact test, the latter is more appropriate if the number of cells on the variable of interest is less than 5,

which is the case for all our categorical variables. The difference is called statistically significant if *p* < 0.05.

The softwares used on the computer are the SPSS version 16 and the STATA version 10. The test used to have homogeneous groups of donors for each variable of interest is the *Cluster analysis*. Concerning the recipients, this test has not been used since the two selected groups, after application of exclusion criteria, were homogeneous.

RESULTS

Were identified in our center 48 adult recipients of living open donors (OR) and 39 adult recipients of living laparoscopic donors (LR). Given the exclusion criteria, were considered in our study 45 OR and 36 LR who were homogeneous: differences in age, sex and body mass index were not statistically significant (See Table I). Both groups of recipients were under the same immunosuppressive regimen: mycophenolate mofetil, prednisone and calcineurin inhibitor.

Were identified in our center 53 open adult donors (OD), including 5 donors for pediatric recipients, and 42 adult laparoscopic donors (LD), including 3 donors for pediatric recipients. Both OD and LD groups were not the same for each variable. Indeed, donors who met the exclusion criteria were not the same for the selected variable. The number of donors was subsequently modified in each variable to have homogeneous groups in terms of age, sex and body mass index (See Tables II & III). The results for recipients and donors were summarized in Table IV & Figure 1.

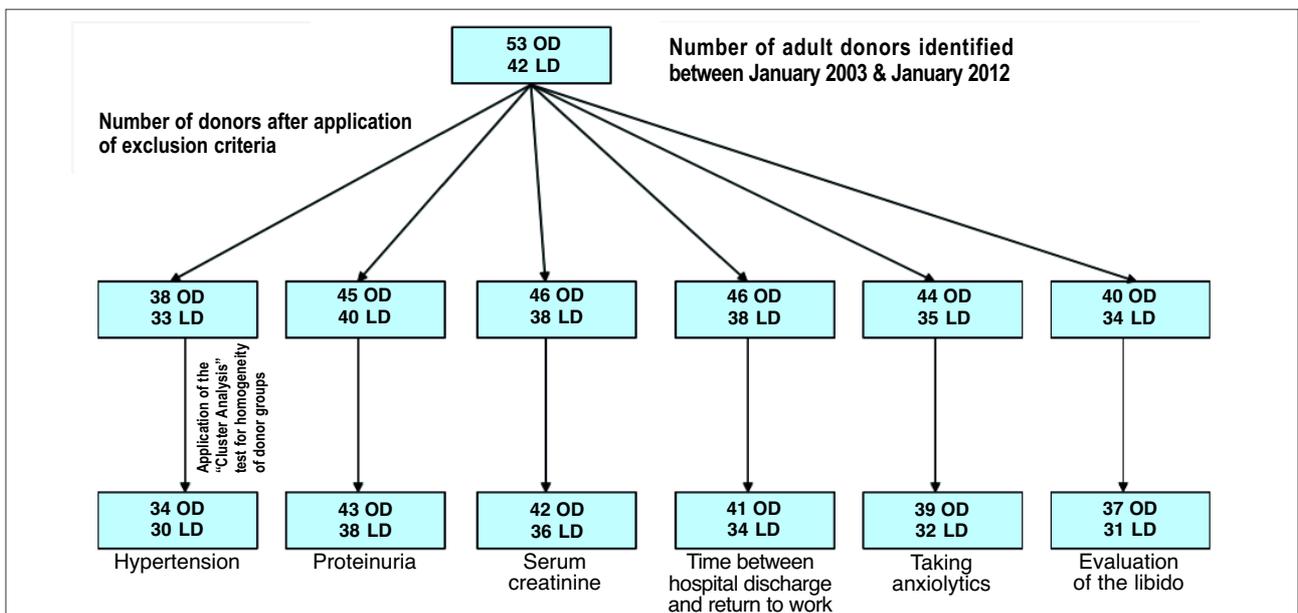


TABLE II. METHOD of SELECTION of DONORS

TABLE III CHARACTERISTICS of SELECTED DONORS ACCORDING to the VARIABLE of INTEREST

Variables	Number of donors and <i>p</i> value	Age ± DS and <i>p</i> value	Sex (M/F) and <i>p</i> value	BMI ± DS (kg/m ²) and <i>p</i> value
Hypertension	34 OD	OD : 39 ± 6	OD : 22/12	OD : 25.8 ± 2.2
	30 LD	LD : 38 ± 7	LD : 14/16	LD : 24.9 ± 2.7
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant
Proteinuria	43 OD	OD : 38 ± 8	OD : 24/19	OD : 25.7 ± 2.4
	38 LD	LD : 39 ± 4	LD : 15/23	LD : 26.1 ± 1.7
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant
Serum creatinine	42 OD	OD : 38 ± 8	OD : 24/18	OD : 25.7 ± 2.4
	36 LD	LD : 39 ± 4	LD : 15/21	LD : 26.1 ± 1.7
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant
Time between hospital discharge & return to work	41 OD	OD : 36 ± 5	OD : 18/23	OD : 25.3 ± 1.5
	34 LD	LD : 37 ± 6	LD : 13/21	LD : 24.9 ± 2.1
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant
Taking anxiolytics	39 OD	OD : 39 ± 6	OD : 11/20	OD : 25.8 ± 2.2
	32 LD	LD : 40 ± 4	LD : 14/18	LD : 24.9 ± 2.7
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant
Evaluation of the libido	37 OD	OD : 35 ± 4	OD : 20/17	OD : 24.8 ± 2.1
	31 LD	LD : 34 ± 4	LD : 16/15	LD : 23.9 ± 1.3
	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant	<i>p</i> not significant

BMI: body mass index

TABLE IV RESULTS of ORGANIC and PSYCHOLOGICAL DONORS COMPLICATIONS in the LONG TERM

Results	Hypertension occurrence in the 1 st year post-op (%)	Proteinuria appearance at 12 ± 2 months post-op (%)	Serum creatinine at 12 ± 2 months post-op (µmol/L)	Time between hospital discharge and return to work (week)	Libido evaluation at 6 months post-op (%)	Taking anxiolytics at 6 months post-op (%)
LD Number	30	38	36	34	31	32
OD Number	34	43	42	41	37	39
Mean or proportion of the variable in LD	13	24	90.81	5.15	19	38
Mean or proportion of the variable in OD	15	26	94.43	8.05	22	56
Confidence interval			[- 11.395 ; 4.156]	[- 3.787 ; - 2.004]		
<i>p</i> value	0.524 ^F	0.608 ^F	0.353 ^t	< 0.001 ^t	0.562 ^F	0.22 ^F

LD: laparoscopic donor OD: open donor *p* value^F: Fischer test *p* value^t: X²

Warm ischemia time

The mean warm ischemia time in LR was significantly higher than that found in OR (175.54 vs. 44.67 seconds). This difference has been proven statistically (*p* < 0.001).

Short-term renal function in recipients

In LR group, the mean serum creatinine at ± J5 post-op was slightly higher than that found in the OR group (1.54 vs 1.50 mg/dl). However, this difference was not statistically significant (*p* = 0.781). Delayed graft function was observed in two LR (2.63 and 2.78 mg/dl) and one OR (2.52 mg/dl), or 7% of LR and 3.33% of OR. The statistical difference was not significant (*p* = 0.605).

Long-term renal function in recipients

In the LR group, the mean serum creatinine at 6 months post-op was slightly lower or almost identical to that

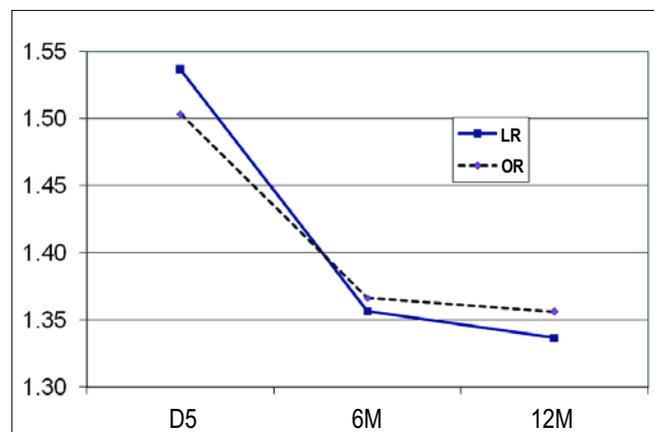


FIGURE 1
Serum creatinine (mg/dl) in recipients

found in the OR (1.36 vs 1.37 mg/dl). No statistical difference was observed ($p = 0.871$) between the two groups. At 12 months, the mean serum creatinine in LR was 1.36 mg/dl, slightly higher than that found in the OR (1.34 mg/dl). The statistical difference in this case is not significant ($p = 0.569$).

Occurrence of hypertension among donors

In the LD group, the occurrence of hypertension during the first year post-op was found in 4 donors (13%). This is lower than what was found in the OD group: 5 OD (15%) had hypertension during the first year. However, the difference was not statistically significant ($p = 0.524$).

Appearance of proteinuria in donors

Appearance of proteinuria at 12 ± 2 months post-op has been reported in 9 LD and 11 OD. The proportion is slightly higher in case of OD (26% vs 24%). The statistical test did not indicate the presence of a significant difference ($p = 0.608$).

Serum creatinine values

The average serum creatinine at 12 ± 2 months in OD were $94.43 \mu\text{mol/L}$, greater than that found in LD ($90.81 \mu\text{mol/L}$). However, the difference was not statistically significant ($p = 0.353$).

Taking anxiolytics

Taking anxiolytics at 6 months post-op was rated higher in OD compared to LD in terms of numbers and proportions: 12 LD (38%) vs. 22 OD (56%). However, statistical tests showed no significant difference ($p = 0.22$).

Return to work

The average time between hospital discharge and return to work was 5.15 weeks in LD, significantly lower than that found in OD (8.05 weeks). Indeed, the statistical difference was highly significant ($p < 0.001$).

Evaluation of libido

The state of decreased libido at 6 months post-op was found in 6 LD (19%). These values are lower than those found in OD (8 OD, 22%). However, the statistical test showed no significant difference ($p = 0.562$).

DISCUSSION

A living donor is not considered a real patient. All the technological advances in minimally invasive surgery have been used on the donor to have better results for cosmetic impact, postoperative pain, lumbotomy complications (hernia, pneumothorax, rib resection, etc.) [4], return to work and physical activity, without missing the principles of open surgery and without altering renal function in the recipient.

Our retrospective cohort study shows that long-term renal function in patients receiving laparoscopic living donor kidney is not statistically different from that found

in recipients of open living donor. This conclusion is supported by the value of serum creatinine assessed at 6 and 12 months post-op. In fact, no current study, including recent data from the UNOS (U.S. United Network for Organ Sharing) [7] showed the superiority of long-term renal function in recipients of open living donor. By cons, Goel *et al.* [8] noted that the long-term renal function in cases of laparoscopic nephrectomy is better than open nephrectomy. However, this result could be affected, as Goel noted in his study, by a difference on the nephrotoxicity of calcineurin inhibitors used in each group. In sum, these results suggest that, despite mechanical aggression suffered by the laparoscopic living donor graft (warm ischemia time, high positive pressure pneumoperitoneum), this latter keeps a proper long-term function. Indeed, the study by Brennan *et al.* [9], who compared the long-term renal function among a group of recipients who had delayed graft function (serum creatinine ≥ 3.0 to 5 days post-op) and another group without delayed graft function, no significant difference was noted in the creatinine clearance at one year. Note that in our study, the short-term renal function (serum creatinine value at 5 days post-op) in recipients of living laparoscopic donor was not statistically different from that found in recipients of living open donor despite warm ischemia time higher in the first group. This calls into question the actual effect of early aggression suffered by the kidney of laparoscopic donors. Our result is identical to that found in several studies [10-11], highlighting the lack of difference in renal function between the two groups of recipients.

The occurrence of hypertension, proteinuria, the aspect of the libido and the need of taking anxiolytics were not statistically different during the first year post-op in the two groups of donors. Indeed, there are no comparative studies on this topic today and against which we could discuss the results. What is known in our literature review is that the psychological impact of donor nephrectomy in the long term was found positive with improved sense of well-being and enhanced self-esteem, especially if the transplantation was without complication in the recipient [12-13]. However, given the benefits of laparoscopic donor (less pain, shorter hospital stay, etc.), we have estimated a difference in their favor; this was not the case according to our analysis.

CONCLUSION

In our center, laparoscopic live donor nephrectomy is similar to the open technique concerning renal graft function in short and long term. For donors, and outside the benefits of laparoscopic technique, the organic and psychological complications were similar; medical monitoring of the donors of the two groups is important given the potential risk they might face. The technique of laparoscopic nephrectomy is not easy to learn and should be offered in specialized centers so that we can achieve comparable results.

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